

In the Claims

1-41 (Canceled).

42 (New). A composition of matter comprising:

- a) an isolated polypeptide having notch-like activity selected from the group consisting of: 1) the amino acid sequence recited in SEQ ID NO: 2; 2) the mature form of the polypeptide whose sequence is recited in SEQ ID NO: 2 (SEQ ID NO:4); 3) active variants of the amino acid sequence of SEQ ID NO: 2, wherein any amino acid specified in the chosen sequence is non-conservatively substituted, provided that no more than 15% of the amino acid residues in the sequence are so changed; and 4) the active fragment, precursor, salt, or derivative of the amino acid sequences given in 1), 2), or 3);
- b) an isolated polypeptide that is a naturally occurring allelic variant of the sequence given by SEQ ID NO: 2 or SEQ ID NO:4;
- c) an isolated polypeptide that is a naturally occurring allelic variant of the sequence given by SEQ ID NO: 2 or SEQ ID NO:4, wherein the variant is the translation of a single nucleotide polymorphism;
- d) a polypeptide as set forth in a) or b) or c), wherein the polypeptide binds specifically an antibody or a binding protein generated against SEQ ID NO: 2 or SEQ ID NO:4 or a fragment thereof;
- e) a fusion protein comprising a polypeptide as set forth in a) or b) or c) or d);
- f) an antagonist of a polypeptide as set forth in a) or b) or c) or d), wherein said antagonist comprises an amino acid sequence resulting from the non-conservative substitution, the deletion or both the non-conservative substitution and deletion of one or more residues into the corresponding polypeptide;
- g) a ligand which binds specifically to a polypeptide a) or b) or c) or d);

h) a polypeptide a) or b) or c) or d) or e), wherein said polypeptides are in the form of active conjugates or complexes with a molecule chosen amongst radioactive labels, fluorescent labels, biotin, or cytotoxic agents;

i) a peptide mimetic designed on the sequence or the structure or the sequence and structure of a polypeptide as set forth in a) or b) or c) or d);

j) an isolated nucleic acid encoding for an isolated polypeptide selected from the group consisting of:

- 1) polypeptides as set forth in a) or b) or c) or d);
- 2) a fusion protein comprising a polypeptide as set forth in a) or b) or c) or d); or
- 3) an antagonist of a polypeptide as set forth in a) or b) or c) or d), wherein said antagonist comprises an amino acid sequence resulting from the non-conservative substitution, the deletion or both the non-conservative substitution and deletion of one or more residues into the corresponding polypeptide;

k) an isolated nucleic acid sequence consisting of SEQ ID NO: 1, or the complement of said DNA sequence;

l) a purified nucleic acid which:

- 1) hybridizes under high stringency conditions; or
- 2) exhibits at least about 85% identity over a stretch of at least about 30 nucleotides with a nucleic acid selected from the group consisting of SEQ ID NO: 1, or a complement of said DNA sequence;

m) a vector comprising a nucleic acid as set forth in j) or k) or l);

n) a polypeptide encoded by the nucleic acid of j) or k) or l);

o) a host cell comprising a vector or nucleic acid as set forth in j) or k) or l) or m);

p) a transgenic animal cell comprising a vector or nucleic acid as set forth in j) or k) or l) or m) and having enhanced or reduced expression levels of a polypeptide as set forth in a) or b) or c) or d);

q) a transgenic non-human animal that has been transformed to have enhanced or reduced expression levels of a polypeptide as set forth in a) or b) or c) or d);

r) a compound that enhances the expression level of a polypeptide as set forth in a) or b) or c) or d) in a cell or animal; or

s) a compound that reduces the expression level of a polypeptide as set forth in a) or b) or c) or d) in a cell or animal.

43. (New) The composition of matter according to claim 42, wherein said composition of matter comprises a polypeptide, peptide mimetic, nucleic acid, cell, or compound that enhances or reduces the expression of a polypeptide and a pharmaceutically acceptable carrier.

44. (New) The composition of matter according to claim 42, wherein the fusion protein further comprises one or more amino acid sequence selected from the protein sequences: membrane-bound protein, immunoglobulin constant region, multimerization domains, extracellular proteins, signal peptide-containing proteins, or export signal-containing proteins.

45. (New) The composition of matter according to claim 42, wherein the ligand antagonizes or inhibits the notch-like activity of a polypeptide.

46. (New) The composition of matter according to claim 45, wherein the ligand is a monoclonal antibody, a polyclonal antibody, a humanized antibody, an antigen binding fragment, or the extracellular domain of a membrane-bound protein.

47. (New) The composition of matter according to claim 42, wherein said vector comprises a nucleic acid molecule that is operatively linked to expression control sequences allowing expression in prokaryotic or eukaryotic host cells of the encoded polypeptide.

48. (New) A method for determining the activity and/or the presence of a notch-like polypeptide in a sample comprising:

a) providing a protein-containing sample;

b) contacting said sample with a ligand that specifically binds to a polypeptide comprising:

- 1) an isolated polypeptide having notch-like activity selected from the group consisting of: i) the amino acid sequence recited in SEQ ID NO: 2; ii) the mature form of the polypeptide whose sequence is recited in SEQ ID NO: 2 (SEQ ID NO:4); iii) active variants of the amino acid sequence of SEQ ID NO: 2, wherein any amino acid specified in the chosen sequence is non-conservatively substituted, provided that no more than 15% of the amino acid residues in the sequence are so changed; and iv) the active fragment, precursor, salt, or derivative of the amino acid sequences given in i), ii), or iii);
- 2) an isolated polypeptide that is a naturally occurring allelic variant of the sequence given by SEQ ID NO: 2 or SEQ ID NO:4;
- 3) an isolated polypeptide that is a naturally occurring allelic variant of the sequence given by SEQ ID NO: 2 or SEQ ID NO:4, wherein the variant is the translation of a single nucleotide polymorphism; or
- 4) a polypeptide as set forth in a) or b) or c), wherein the polypeptide binds specifically an antibody or a binding protein generated against SEQ ID NO: 2 or SEQ ID NO:4 or a fragment thereof ; and

c) determining the presence or said ligand bound to said polypeptide.

49. (New) A method of using the composition of claim 42 for a) producing cells capable of expressing a polypeptide; b) making a polypeptide; c) the treatment of a disease; d) the preparation of pharmaceutical compositions; e) the screening candidate compounds; f) identifying a candidate compound; or g) determining the presence or the amount of a transcript or of a nucleic acid.

50. (New) The method according to claim 49, wherein said method comprises genetically engineering cells with a vector or a nucleic acid comprising:

a) an isolated nucleic acid encoding for an isolated polypeptide selected from the group consisting of:

- 1) an isolated polypeptide having notch-like activity selected from the group consisting of: i) the amino acid sequence recited in SEQ ID NO: 2; ii) the mature form of the polypeptide whose sequence is recited in SEQ ID NO: 2 (SEQ ID NO:4); iii) active variants of the amino acid sequence of SEQ ID NO: 2, wherein any amino acid specified in the chosen sequence is non-conservatively substituted, provided that no more than 15% of the amino acid residues in the sequence are so changed; and iv) the active fragment, precursor, salt, or derivative of the amino acid sequences given in i), ii), or iii);
- 2) an isolated polypeptide that is a naturally occurring allelic variant of the sequence given by SEQ ID NO: 2 or SEQ ID NO:4;
- 3) an isolated polypeptide that is a naturally occurring allelic variant of the sequence given by SEQ ID NO: 2 or SEQ ID NO:4, wherein the variant is the translation of a single nucleotide polymorphism;
- 4) a polypeptide as set forth in 1) or 2) or 3), wherein the polypeptide binds specifically an antibody or a binding protein generated against SEQ ID NO: 2 or SEQ ID NO:4 or a fragment thereof; or
- 5) a fusion protein comprising a polypeptide as set forth in 1) or 2) or 3) or 4);

b) an isolated nucleic acid sequence consisting of SEQ ID NO: 1, or the complement of said DNA sequence;

c) a purified nucleic acid which:

- 1) hybridizes under high stringency conditions; or
- 2) exhibits at least about 85% identity over a stretch of at least about 30 nucleotides with a nucleic acid selected from the group consisting of SEQ ID NO: 1, or a complement of said DNA sequence; or

d) a vector comprising a nucleic acid as set forth in a) or b) or c).

51. (New) The method according to claim 49, wherein said method comprises a method for making a polypeptide comprising culturing a transformed host cell under conditions in which the nucleic acid or vector is expressed, and recovering the polypeptide encoded by said nucleic acid or vector from the culture.

52. (New) The method according to claim 49, wherein said method comprises the treatment of a disease needing an increase in the notch-like activity that comprises the administration of a therapeutically effective amount of a polypeptide, a peptide mimetic, a nucleic acid, a cell, or a compound as set forth in claim 42.

53. (New) The method according to claim 49, wherein said method of treatment comprises the administration of a therapeutically effective amount of an antagonist, a ligand, or of a compound as set forth in claim 42.

54. (New) The method according to claim 49, wherein said method for screening candidate compounds effective to treat a disease related to the notch-like polypeptides comprises:

- a) contacting a cell, a transgenic animal cell, or a transgenic non-human animal having enhanced or reduced expression levels of the notch-like polypeptide, with a candidate compound and
- b) determining the effect of the compound on the animal or on the cell.

55. (New) The method according to claim 49, wherein said method for identifying a candidate compound as an antagonist/inhibitor or agonist/activator of a notch-like polypeptide comprises:

- a) contacting said polypeptide, said compound, and a mammalian cell or a mammalian cell membrane capable of binding the polypeptide; and
- b) measuring whether the molecule blocks or enhances the interaction of the polypeptide, or the response that results from such interaction, with the mammalian cell or the mammalian cell membrane.

56. (New). The method according to claim 49, wherein said method for determining the presence or the amount of a transcript or of a nucleic acid encoding a notch-like polypeptide comprises:

- a) providing a nucleic acids-containing sample;
- b) contacting said sample with a nucleic acid as set forth in claim 42; and
- c) determining the hybridization of said nucleic acid with a nucleic acid into the sample.